ENDOTEC

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August 25, 2005

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Office of Device Evaluation
CDRH
9200 Corporate Blvd.
Rockville, MD 20850

Re: Docket Number 2004P-0457/CCP 1: Reclassification of Non-constrained, Mobile-Bearing Ankle Prosthesis

Dear Mr. Phillips:

Endotec would like to thank the staff of the FDA for their review of this complex petition for reclassification. Their constructive criticism has been the basis of a much improved amended petition.

In response to the FDA letter dated June 20, 2005 please find attached an updated version of the reclassification of non-constrained, mobile-bearing ankle prostheses reflecting the concerns itemized in the letter. We have integrated more recent references to bring the agency up to date with current publications and have added sections to the Special Controls.

Your request for additional information, comments and suggestions cited in the above-mentioned letter were reviewed and we have formulated the following response:

With regard to the proposal by the FDA that we consider including cemented devices in the reclassification we feel that there is insufficient evidence to support reclassification of cemented devices. Almost all studies that we rely on to support this petition are of cementless devices. The little information available comparing cemented and cementless devices indicates that cemented fixation may be inferior to cementless in moderate and longer-term use. Since talar subsidence is the most common complication encountered in the better performing designs we are reluctant to propose reclassification of devices which may compromise fixation.

With regard to the numbered items of the letter:

1a) We have revised the device description on pages 9 and 10 of the petition such that it encompasses all, if not most, of the mobile bearing devices, and thus mobile bearing device types, that are currently on the international market, as far as is known by Endotec. Further, if there are mobile bearing types that are not covered by the petition there is no evidence known to us that would support their reclassification. We have reviewed and revised the petition to make it clearer that it encompasses most available device types.

1b) We have reviewed and revised the sections on risks of pp 26-42 to insure they cover all types encompassed in this petition. And we have revised the special

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controls, particularly in Sections 7 and 10 to describe how testing and other controls mitigate these risks. Section XIV (p 76-77) has been added to provide the rationale for the special controls and to correlate the controls to clinical safety.

As far as we know there are no standards that are specific to mobile bearings and thus we could not include them. As far as we are aware there are no standards for ankle device testing. We have, therefore, developed guides for testing ankles (see Appendix J – Ankle Testing Guidance Documents; P-001 and P-002 which are based on the ASTM F 1715 and F 1800 standards respectively.

Although there are anatomical and biomechanical differences between the knee and ankle there are also many similarities. Further an understanding of the differences that do exist can be helpful in evaluating ankle devices based on experience with the knee, which is substantial. For example since knee devices use materials similar to ankles knee data can provide useful background information on the expected behavior of these materials in ankles. We have, however, removed test results on knee and hip devices which we felt were not useful.

We have modified and added special controls (see Annex A1 and Appendix X1 of P-001 and Appendix X1 of P-002) to correlate preclinical test with clinical results and information on whether these revisions and additions will adequately control risks associated with mobile bearing ankles of the type encompassed by the petition. There is a further discussion of such controls below.

2. We have removed the results of the IDE study from the petition.

3. We have provided a financial disclosure.

4a) The content of the petition has been amended to include information described in the Supplemental Data sheet.

i. A summary of the reasons for reclassification have been provided in sections VI. Introduction (pages 7-8) and X. Current Classification: 2. Basis for disagreement with the Current Classification.

ii. A summary of clinical data on which the petition is based is provided in section XIV. Summary of Clinical Findings.

iii. An identification of risks presented by the device is provided in section XII. Control of Risks.

iv. A priority for application requirements has been provided in Appendix K – Special Controls.

v. Not Applicable

vi. Not Applicable

vii. An identification of needed restrictions has been provided in Appendix K – Special Controls.

viii. Existing standards have been provided in section XII. Control of Risks (page 27) and Appendix E – Special Controls: 8. Controls (page 13-14)

4. b) Representative data and information that are unfavorable to the petition is not known to us. However, if it does exist it is included in the presentation and discussion of the complications or results of the clinical studies of the B-P device cited in the reference section of the petition.

5. The device is indicated only for patients with viable malloli and ankle ligaments. If the "patients have attenuated ligaments and tendons (e.g., osteoarthritic cases) or deformity due to autoimmune destruction of bone and surrounding soft tissue (e.g. rheumatoid arthritis cases) or deformity of the bony structures leading to altered strength of ligamentous or tendinous structures (e.g. post trauma or avascular necrosis related to arthritis) such that essentially normal ankle stability is not present and cannot be reconstructed then the device is contraindicated for such patients. We have revised the petition (see Appendix D – Inserts and Labeling) and Special Controls in section 7d. and 8. to insure that this is clear.

Further we have added special controls on mobile bearing ankle stability with evidence that these controls can identify clinically successful ankle types in section 7c. It should be noted that controls based on evidence sufficient to show that they will indicate clinically successful mobile bearing types limit the number of types satisfying these controls.

It should be noted that the presence of viable collateral ligaments is not a unique requirement of these mobile bearing ankle types. Such ligaments are needed in any semi-constrained device.

5a) The petition has been revised (see p 40, l 4-1) to show the basis of the M/L, A/P bearing to talar component motion resistance and torsional properties. Testing is not needed to establish such resistance and characteristics analysis is sufficient. Ref. 24 describes device stability and dislocation resistance in detail. A special control (section 7c.) on stability which addresses this concern and that of item 5.c) are provided.

5b) This concern is addressed in section 7h. and 8 of the special controls.

5c) The petition has been revised (see p 39 – 40 through l 3) to clarify the inversion-eversion properties of the subject device. The M/L, A/P and torsional stability properties of the bearing have been addressed as descried in 5a) above. This concern is addressed in section 7c. of the Special Controls.

6. This concern is addressed in section 7c. of the Special Controls.

6a) The Collier retrieval group at Dartmouth have shown that "backside" damage is more extensive in fixed bearings than mobile bearings. Such damage also occurs in acetabular cup. We know of no controls on such damage in controls associated with Class II hips or knees. One wonders, therefore, why such a control is not used elsewhere? Nevertheless we feel such control is needed. This control has been included by requiring contact stress evaluation of the secondary articulation "backside" surfaces (p 10, l 5-6) of section 7b.i and requiring any wear test by ankle simulator to include axial rotation and AP translation to allow subject the secondary articular surface to sliding and thus wear (p11, l 4-5) in section 7b.ii.

6b) A minimum thickness control is needed for two primary reasons. First to reduce stresses resulting from the stiffening effect of metal backing in incongruent contact articulation. Secondly a minimum is needed to provide for loss of thickness resulting from wear. Based on a thickness 3mm, used in most of the bearings of the successful B-P design, a minimum thickness of 3mm is required. This is specified in section 7b.iv of the Special Controls.

7a) The labeling requirements suggested have been included in the Special Controls in section 10 page 14. Also, an example of the packaging insert has been provided in Appendix D.

7b) The surgical procedure, Appendix C, has been revised (see section 4b) to reflect the suggestions of items i-iv and the petition has been revised to add a discussion of bone resection in section XI.h. A special control has been added to deal with excessive bone resection in section 7h. The "Directions for Use" of section 10 of the special controls has been expanded to reflect your concerns.

8. A suggested training program included in Appendix H. The "Directions for Use" of section 10 of the special controls has been expanded to reflect this concern.

9. The "Directions for Use" of section 10 of the special controls has been expanded to reflect this concern.

10. A special control added on the matter in section 7d.

11. All reference to the Endotec clinical trial data has been removed. However, the disparity between the device removals reported on page 27 and compassionate use requests can be explained as the device removals reported in the petition included only those devices removed and not those revised.

12. The wording of the petition has been modified (p33 3rd paragraph). The word "proven" is too strong. The word "indicate" is more appropriate. The citation of Ref. 5 was incorrect. The hard copy reference 40 of the earlier submission (now Ref. 38) had been supplied in an earlier submission of this petition. This latter reference, however, really does not supply useful comparative data on cemented vs. uncemented ankle devices. Better references, Refs. 11 and 15 are now used to substantiate our statement.

13. Hard copies of these references were given to the FDA as part of the submission of 2001.

14. All moderate and longer term studies not involving Dr. Buechel that we are aware of are described in References 10-13, 40, 50-53 and 80.

15. All of the studies of the LCS and B-P ankles cited used porous coating in the range specified. The studies of Refs. 5, 10, 12, 17, 51-53 and Appendix I include radiological analyses of the bone prostheses interfaces. No significant problems of ingrowth are reported. There is supportive clinical evidence that the specified porous configuration is safe.

Further there is no reason to believe that there is any significant difference in ingrowth properties associated with bones of the ankle and hip or knee. Further any difference should be less than the difference between dogs, which were used as the model for evaluating porous coating configurations, and humans to which these evaluations have been applied.

16. The shallow sulcus design was made by DePuy and DePuy initiated a clinical trial of this device in the early 1980's. They would have supplied the information you need in the application to run an IDE. Any engineering drawings that exist are DePuy drawings which we may not have and which we could not make available to you without their permission. The petition has been revised to expand the discussion of the Mark I device and the differences between it and the Mark II on pages 15-17 particularly as shown in figs 7 and 9. The Mark II engineering drawings are in Appendix A.

17. We have revised our petition (see p 16, l 5-7) on this matter, included Ref. 21 on blood supply to the talus and Appendix G on the effect of implantation of the B-P talar component on blood supply. Special control has been added in 7.h.

18. It is difficult to ascertain from the literature that was published on non-B-P ankles whether this same patient results were reported in multiple data sources. As far as the B-P ankle system is concerned the same patient population was reported for Dr Buechel in Refs 5, 9, 17, 42 and 79. Dr Keblish in Ref 28 used some of Dr Buechel's patients reported in Ref 17. There may be an overlapping of he populations used by Dr Doets in Refs. 12, 40, 51 and 53. (See section XII Summary of Clinical Findings and XVI Bibliography).

All Pre-clinical testing, in vivo testing and analysis cited in this petition were performed on one design: the Buechel-Pappas Ankle System Mark II (Deep Sulcus) with the exception of the finite element analysis of the plate which was done for the original Mark I. This analysis is applicable to the Mark II since they are so similar.

An explanation of specific designs linked with the clinical data is presented in both reference abstracts and tables within this petition (See section XII Summary of Clinical Findings: 4. The predecessor: B-P Total Ankle System (Shallow Sulcus) and section 5. B-P Total Ankle System (Deep Sulcus).

19. The petition has been revised to add discussion of the Agility device (see p66 2nd paragraph and p 75 2nd paragraph). Additional demographic, diagnosis and survival end point information, where available, have been added to the reference abstracts of Section XIV of the petition and to the data presentation tables (see pages 65,72 and 74).

20-22. These matters have been attended to in this amended petition.

Sincerely,

Michael J. Pappas

Michael J. Pappas Ph.D., P.E.
President, Endotec

Encl.